Masten.Scott

From: Nathan Harris
Sent: 2000, December, 20 - 11:31 AM
To: masten@niehs.nih.gov
Subject: comments on nominated chemicals

Dr. Scott Masten, NIEHS/NTP

Dear Dr. Masten,

I am sending comments about several chemicals nominated for toxicological studies. These chemicals were tested against our genotoxicity databases (A2E and A2I) using our Multicase QSAR software. Validation studies show both databases have predictive capability of about 85% (true result in 85% of tests). A positive (active) prediction indicates a likelihood of genotoxicity, a negative (inactive) prediction indicates the compound is not genotoxic. Two predictions for the dyes D&C Red No. 27 and 28 are marked inconclusive, because these molecules contain functionality not present in the learning set. Thus our system cannot make a prediction for these two molecules.

CAS NR	NAME	A2E	
55268-75-2	cefuroxime	inactive	
81103-11-9	clarithromycin	inactive	i
13473-26-2	D&C Red No. 27	inconclusive	ina
18472-87-2	D&C Red No. 28	inconclusive	inconcl
99-97-8	N,N-dimethyl-p-toluidine	active	in

Notes:
[1] These tests don't take account of possible metabolic activation of the chemicals. For example the last three chemicals are likely to be oxidized in mammals by cytochrome P450.
[2] The A2E database consists of 784 organic chemicals compiled by Ashby and coworkers, targeting structural alerts for DNA reactivity. See Zeiger E, Ashby J, Bakale G, Enslein K, Klopman G, Rosenkranz HS. "Prediction of Salmonella mutagenicity." Mutagenesis 1996; 11(5):471-484. Ashby J, Paton D. " The influence of chemical structure on the extent and sites of carcinogenesis for 522 rodent carcinogens and 55 different human carcinogen exposures." Mutat Res. 1993 Mar;286(1):3-74.
[3] The A2I database consists of 2236 organic chemicals tested for mutagenicity in Salmonella typhimurium compiled from Genetox, NTP, and FDA sources.
[4] For details about the MCASE program see the following reference: Klopman G "MULTICASE 1. A Hierarchical Computer Automated Structure Evaluation Program" Quant Struct-Act Relat. 11: 176-184, 1992.

I hope these comments will be useful

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